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Alum-functionalized graphene oxide nanocomplexes for effective anticancer vaccination

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Abstract

Aluminum-based adjuvant (e.g., aluminum oxyhydroxide (AIO(OH)), known as the commercial Alhydrogel® (Alum)) is the first adjuvant to be used in human vaccines. Although Alum shows a robust induction of antibody-mediated immunity, its weak stimulation of cell-mediated immunity makes it a questionable adjuvant for cancer immunotherapy. Herein, we described a novel formulation of Alum-based adjuvant by preparing AIO(OH)-modified graphene oxide (GO) nanosheets (GO-AIO(OH)), which, in addition to maintaining the induction of humoral immune response by AIO(OH), could further elicit the cellular immune response by GO. Similar to Alum, GO-AIO(OH) vaccine formulation could be constructed by the incorporation of antigen using a facile mixing/adsorption approach. Antigen-loaded GO-AIO(OH) nanocomplexes facilitated cellular uptake and cytosolic release of antigens and promoted DC maturation, thereby eliciting higher antigen-specific IgG titers, inducing robust CD4⁺ and CD8⁺ T lymphocyte response, and inhibiting tumor growth in vivo. Furthermore, by employing tumor cell lysate-based cancer vaccines, GO-AIO(OH) nanocomplexes led to significant inhibition of tumor growth and can be implemented as a personalized treatment strategy for cancer vaccine development. Overall, GO-AIO(OH) nanocomplexes described herein may serve as a facile and efficient approach for effective anticancer vaccination. STATEMENT OF SIGNIFICANCE: Herein, we described a novel formulation of aluminum-based adjuvant by preparing aluminum oxyhydroxide (AIO(OH)) (known as "Alum")-modified graphene oxide (GO) nanocomplexes (GO-AIO(OH)), which, in addition to maintaining the induction of humoral immune response by AIO(OH), could further elicit the cellular immune response by GO. GO-AIO(OH) nanocomplexes can be prepared easily and in large scale by a chemical precipitation method. Similar to "Alum," antigen-loaded GO-AIO(OH) vaccine formulation could be constructed by the incorporation of antigen using a facile mixing/adsorption approach. The very simple and reproductive preparation process of vaccines and the powerful ability to raise both humoral and cellular immune responses provide a novel approach for improving cancer immunotherapy efficacy.

Keywords: Adjuvant; Aluminum oxyhydroxide; Cancer immunotherapy; Graphene oxide; Vaccine.

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